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(54) Coated lipid-containing compositions

(57) Solid tablet compositions comprising a lipid-containing core composition and three coatings, said coatings comprising:

(1) a base coating, in direct contact with the core composition, comprising a binder and a sugar material;

(2) a sealant coating, in direct contact with the base coat coating, comprising a film-forming material; and

(3) a structural coating, in direct contact with the sealant coating, comprising a sugar material.

Among the preferred lipid-containing compositions of this invention are chewable tablets useful for the treatment of upper gastrointestinal disorders, such as an antacid composition containing from 10% to 65% of an acid neutralizing material.

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SPECIFICATION

Coated lipid-containing compositions

BACKGROUND OF THE INVENTION

This invention relates to coated, solid, lipid-containing compositions useful for oral ingestion by humans and other animals. In particular, it relates to preferred compositions comprising a pharmaceutical active in a coated, lipid-containing matrix. Preferred compositions further relate to highly palatable, storage stable tablets, which are chewable or liquify in the mouth, useful for the treatment of gastrointestinal disorders.

Pharmaceutical compositions may be produced in a variety of dosage forms, depending upon the desired route of administration of the active material. Oral dosage forms, for example, include such solid compositions as tablets, capsules, granules and bulk powders, and such liquid compositions as solutions, emulsions, and suspensions. The particular dosage form utilized may, of course, depend upon such factors as the solubility and chemical reactivity of the pharmaceutical active. Further, the dosage form may be selected so as to optimize delivery of the pharmaceutical active and/or consumer acceptability of the composition.

Tablet compositions offer many advantages, including ease of product handling, chemical and physical stabilty, portability (in particular, allowing ready availability to the consumer when needed), aesthetic acceptabilty, and dosage precision, (i.e., ensuring consistent and accurate doses of the pharmaceutical active). However, liquid formulations may offer advantages in the treatment of certain disorders, such as disorders of the upper gastrointestinal tract, wherein delivery of an active material dissolved or dispersed in a liquid ensures rapid and complete delivery to the afflicted area. In an effort to obtain the therapeutic advantages associated with liquid formulations as well as the broad advantages associated with solids, many chewable tablet formulations have been developed and described in the pharmaceutical literature. See, for example, L. Lachman, et al., *The Theory and Practice of Industrial Pharmacy* (2nd Ed., 1976).

Many such compositions are antacids, for the treatment of gastric hyperacidity and related disorders. Many antacid compositions in liquid form are quite effective due to the ready availability of the antacid active material (which is typically waterinsoluble) suspended in a liquid vehicle. There are also many solid antacid formulations, typicaliy chewable tablets, which are designed to deliver small particles of antacid active to the stomach after chewing of the tablet.

Many chewable tablets, such as antacid tablets, often contain high levels of mannitol or simiar binders as well as methylcellulose, glycine, or other binding agents. Other chewable tablets are described in the literature containing fatty materials. See, for example, U.S. Patent 4,230,693, Izzo, et al., issued October 28, 1980, U.S. Patent 4,327,076, Puglia, et al., issued April 27, 1982, U.S. Patent 4,327,077, Puglia, et al., issued April 27, 1982, U.S. Patent 4,533,543, Morris, et al., issued August 6, 1985, and U.S. Patent 4,581,381, Morris, et al., issued April 8, 1986.

Many such solid antacid formulations fai to offer equivalent efficacy to liquid antacid compositions, for a variety of reasons. For example, the tablets may be incompletely chewed due to poor palatabiity of the composition. This problem is particularly acute with antacids, since the active materials in these products often have a metaliic flavor and an astringent, chalky mouth feel. Such compositions may also have a gummy texture, and are subject to "taste fatigue", i.e., the composition is perceived to be less palatable after ingestion of multiple doses. Further, the binders and other materials used in such chewable tablets may prevent rapid and effective delivery of active materials to the stomach.

Tablet compositions containing fatty materials may also exhibit undesirable handling and storage characteristics. For example, such compositions may melt, or may "leak", when exposed to high tem peratures (i.e., at body temperature or higher). Fat-based tablets may also soften and become physicaliy deformed. These undesirable characteristics may limit the commercial utility of the tablets, due to low-temperature storage or shipping requirements, or by preventing normal carrying and handling by consumers.

It has been found that fat-based tablets with a pharmaceutically-acceptable coating are stable compositions. Many coating techniques are known in the pharmaceutical arts. See, for example, the techniques described in *The Theory and Practice of Industrial Pharmacy*, cited above. However, it has been found that many such techniques may interfere with the preferred palatability of fat-containing tablets. Also, many commonly-used coating materials may be ineffective or otherwise unacceptable for coating fat-containing tablets. For example, coating materials and techniques known in the art may be unacceptable for coating fat-containing tablets, due to expansion of the core composition during melting and re-solidification of the core.

It has been found that lipid-containing compositions that are coated with a three-layer coating of selected coating materials are highly palatable and stable compositions. Such compositions, containing a base coating of sugar materials, a sealant coating of a film forming material, and a structural coating of a sugar material, afford effective coating of lipid-containing compositions,

whie maintaining high palatability. In particular, for example, such coatings do not crack and maintain the physical integrity of the lipid-containing core composition, even at elevated temperatures.

SUMMARY OF THE INVENTION

The present invention provides solid tablet compositions comprising a lipid-containing core composition and three coatings, said coatings comprising:

(1) a base coating, in direct contact with said core composition, comprising a binder and a sugar material;

(2) a sealant coating, in direct contact with said base coat coating, comprising a film-forming material; and

(3) a structural coating, in direct contact with said sealant coating, comprising a sugar material.

The present invention also provides methods for making such coated compositions. Among the preferred lipid-containing compositions of this invention are chewable tablets useful for the treatment of upper gastrointestinal disorders, such as an antacid composition containing from about 10% to 65% of an acid neutralizing material.

DESCRIPTION OF THE INVENTION

The compositions of the present invention comprise a lipid-containing core composition coated with at least three coating layers. Preferred compositions of this invention contain a pharmaceutical active material in the lipid-containing core composition. In addition, the pharmaceutical compositions of the present invention may contain optional pharmaceutically-acceptable components which may modify their physical characteristics and/or therapeutic effects. All components of such compositions must, of course, be pharmaceuticaiy-acceptable. As used herein, a "pharmaceuticaiy-acceptable" component is one which is suitable for use with humans and/or other animals without undue adverse side effects (such as toxicity, irritation and allergic response) commensurate with a reasonable benefit/risk ratio.

Specifically, the compositions of this invention comprise a lipid-containing core composition and three coatings, said coatings comprising:

(1) a base coating, in direct contact with said core composition, comprising a binder and a sugar material;

(2) a sealant coating, in direct contact with said base coating, comprising a film-forming material; and (3) a structural coating, in direct contact with said sealant coating, comprising a sugar material.

Preferably these compositions are comprised of from about 50% to about 90%, more preferably from about 70% to about 90%, of said core composition. (As used herein, all percentages are by weight of total coated composition, unless noted otherwise.) Preferably, the sugar material of the base coating is present at a level of from about 1.5% to about 5%, preferably from about 2% to about 4.5%. The binder material is preferably present at a level of from about 0.5% to about 2%, more preferably from about 0.6% to about 1.2%. Also preferably, the film-forming material is present at a level of from about 0.2% to about 1%, more preferably from about 0.4% to about 0.8%. The sugar material of the structural coating is preferably present at a level of from about 5% to about 30%, preferably from about 10% to about 20%, more preferably from about 10% to about 15%.

Also preferably, the lipid-containing core composition contains a safe and effective amount of a pharmaceutical active material. As used herein, the term "safe and effective amount" refers to the quantity of a component which is sufficient to yield a desired therapeutic response without undue adverse side effects (such as toxicity, irritation or allergic response) commensurate with a reasonable benefit/risk ratio when used in the manner of this invention. The specific "safe and effective amount" will, obviously, vary with such factors as the particular condition that is being treated, the severity of the condition, the duration of the treatment, the physical condition of the patient, the nature of concurrent therapy (if any), and the specific formulation and optional components employed.

The compositions of this invention are preferably provided in unit dosage form. As used herein a "unit dose" is that amount of composition which is intended for consumption by a human or lower animal in a single dose. Unit dosage pharmaceutical compositions of this invention contain an amount of a pharmaceutical active material that is suitable for administration to a human or lower animal subject, in a single dose, according to good medical practice. The coated compositions of this invention preferably contain from abut 0.5 grams to about 2.5 grams, preferably from about 1 gram to about 2 grams of the lipid-containing core composition.

Core Composition

The core composition is comprised in whole or in part of a lipid base material. Preferably the core composition also contains a dispersant material, one or more emulsification materials, and a pharmaceutical active material.

The core composition may be in molded or compressed form. Compressed cores are produced by compression of core components, in a solid or semi-solid mixture. Molded tablets are produced by forming a liquid product mass, i.e., by melting the lipid base material and admixing any optional components, foliowed by pouring into tablet-form molds, and cooling to a solid state. The core compositions of this invention are preferably comprised to facilitate chewing and/or melting in the mouth.

Lipid Material:

The core compositions of the invention contain one or more materials, herein individualiy and in mixtures referred to as "lipid materials", that are substantiaiy water-insoluble, inert, pharmaceutically-acceptable hydrocarbon fats or ois, or their derivatives, or mixtures thereof. The lipid material is preferably present at a level of from about 10% to about 50%, more preferably from about 25% to about 40% of the core composition.

The lipid materials useful herein preferably have a melting point of from about 26°C (80°F) to about 43°C (110°F), more preferably from about 30°C (86°F) to about 38°C (100°F), more preferably from about 32°C (90°F) to about 37°C (99°F). The particular lipid material employed may be selected in order to obtain desired product characteristics. These characteristics include such factors as rheology (mouth feel), appearance, flavor and compatibiity with the pharmaceutical active (if any).

Among the lipid materials useful herein are those which are commercially avaiable and commonly used in confectionery and other food products. Such lipid materials include, for example, cocoa butter, hydrogenated tallow, hydrogenated vegetable ois, and derivatives and mixtures thereof. Hydrogenated vegetable oils (such as hydrogenated palm kernel oi), cocoa butter, and cocoa butter substitutes are among the preferred useful ipid materials. Lipid materials among those useful in this invention are described in the following documents, all incorporated by reference herein: U.S. Patent 2,903,363, Farr, issued September 8, 1959; British Patent Specification 827,176, Best et al., published February 3, 1960; U.S. Patent 3,012,891, Best et al., issued December 12, 1961; U.S. Patent 3,093,480, Arnold, issued June 11, 1963; U.S. Patent 3,492,130, Harwood, issued January 27, 1970; U.S. Patent RE 28,737, Yetter reissued March 16, 1976; European Patent Application 23,062, Cotton et al., published January 28, 1981; U.S. Patent 4,276,322, Padley et al., issued June 30 1981; U.S. Patent 4,283,436, Soeters et al., issued August 31, 1981; U.S. Patent 4,364,868, Hargreaves, issued December 21, 1982; and U.S. Patent 4,581,381, Morris et al., issued April 8, 1986; and U.S. Patent 4,594,259, Baker et al., issued June 10, 1986.

Particularly preferred lipid materials are those that melt sharply at about 33°C (91°F). Such fats which melt "sharply" are those with melting profiles simiar to cocoa butter, which is a solid at ambient temperatures, but is entirely liquid at a point just below body temperature (37°C). A particularly preferred lipid material is described in U.S. Patent 4,594,259, Baker et al., issued June 10, 1986. Solid pharmaceutical compositions containing these particularly preferred materials are described in U.S. Patent Application Serial No. (P&G Case 3570), fied October 6, 1986.

Such particularly preferred compositions contain one or more materials, herein "lipid base materials", which together with all other mono-, di- and tri-glycerides (if any) in the compositions form the "lipid component" of the chewable tablet compositions. The lipid component of the present composition thus preferably contains certain key triglycerides: saturated-oleic-saturated ("SOS"), saturated-unsaturated-unsaturated ("SUU"), unsaturated-unsaturated-unsaturated ("UUU"), saturated-linoelic-saturated ("SLS"), saturated-saturated-oleic ("SSO"), and saturated-saturated-saturated ("SSS") triglycerides, i.e., referring to the chemical structure of the fatty acid moiety of each glyceride in the key triglyceride. As used herein, "S" refers to the stearic ("St") or palmitic ("P") fatty acid residues of the glyceride molecule and ("U") refers to the oleic ("O") or linoleic ("L") fatty acid residues of the glyceride molecule.

Specifically, the lipid component of such particularly preferred composition contains at least about 70% of SOS triglycerides, and from about 4% to about 20% of combined SUU/UUU/SLS triglycerides, where the St:P weight ratio is about 0.8 or less. (These percentages are by weight of the lipid component, not by weight of total composition.) Preferably the lipid component contains about 8% or less of SLS triglycerides, about 9.5% or less of SSO triglycerides, about 2.5% or less of SSS triglycerides, and about 4% or less of other triglycerides. The lipid component of the present invention preferably is comprised entirely of a fat having a low St:P ratio (about 0.2 or less). A POP fat is particularly preferred. A preferred source of POP fat is through a triple stage solvent fractionation of palm oil. This process is described in U.S. Patent 4,588,604, Baker et al., issued May 13, 1986 (incorporated by reference herein).

Optional Core Materials:

The core compositions of this invention may also contain optional components which modify the physical and/or therapeutic effects (for pharmaceuticals) of the composition. Such optional

components may include, for example, emulsifiers, binders, lubricants, glydants, colorants, flavors and sweeteners. Such components are generally described in Marshall, "Solid Oral Dosage Forms", *Modern Pharmaceutics, Volume 7*, (Banker and Rhodes, editors), 359-427 (1979), incorporated by reference herein, and W. Gunsel, et al., "Tablets", *The Theory and Practice of Indus-trial Pharmacy* (L. Lachman, et al., editors, 2 (ed.), 321-358 (1976), incorporated by reference herein.

The core compositions of this invention also preferably contain a hydrophiic material, herein "dispersant material", which serves to aid dispersion of the pharmaceutical active and other materials of the composition in the mouth and/or stomach. The dispersant material is preferably present at a level of from about 10% to about 50%, more preferably from about 20% to about 35% of the core composition.

Many dispersants among those useful herein are known in the pharmaceutical arts. Dispersant materials among those useful herein include sugars (such as sucrose, mannitol, sorbitol, dextrose, maltose, and lactose), starches and starch derivatives, (such as corn starch and maltodextrin), microcrystalline cellulose, and mixtures thereof. Among the preferred dispersant materials useful herein are sucrose, sorbitol, mannitol, and mixtures thereof.

The core compositions of the present invention preferably contain from about 0.1% to about 3.0%, preferably from about 0.8% to about 1.5% (by weight of the core composition), of one or more emulsifiers, i.e., a material (or mixture of materials) which aids in dispersing a liquid in an otherwise immiscible liquid. Many such emulsifiers are known in the pharmaceutical arts. See, for example, M. Riegler, "Emulsions", *The Theory and Practice of Industrial Pharmacy* (L. Lachman, et al., ed. 1976), incorporated by reference herein.

Among the emulsifiers useful herein are the alkyl aryl sulfonates, alkyl sulfates, sulfonated amides and amines, sulfated and sulfonated esters and ethers, alkyl sulfonates, polyethoxylated esters, mono and diglycerides (which also constitute part of the lipid component, described above), diacetyl tartaric esters of monoglycerides, polyglycerol esters, sorbitan esters and ethoxylates, lactylated esters, propylene glycol esters, sucrose esters, and mixtures thereof. Emulsifiers among those useful herein are described in *McCutcheon's Emulsifiers and Detergents, North American Edition* (1983), incorporated by reference herein.

Emulsifiers may be characterized by their hydrophilic/lipophiic behavior. This behavior can be numericaliy expressed for a given emulsifier by its hydrophiic-lipophilic balance (HLB). The HLB value of an emulsifier can be determined experimentally or computed (particularly for polyoxyethylene ethers) from its structural formula. In general, emulsifiers with high HLB values are more hydrophiic, and tend to favor formation of oi-in-water emulsions, as opposed to emulsifiers with lower HLB values.

The emulsifiers incorporated into the cores of pharmaceutical compositions of this invention preferably have an average HLB of at least about 8, preferably at least about 10. As used herein, the term "average HLB" refers to the weighted average of the HLB of all emulsifiers in the composition, i.e.,

$$\text{total HLB} = \frac{HLB_1 \times Wt\%\ E_1, + HLB_2 \times Wt\%\ E_2 + \ldots HLB_n \times Wt\ \%\ E_n}{Wt\%\ E_1 + Wt\%\ E_2 + \ldots Wt\%\ E_n}$$

wherein the composition contains "n" number of emulsifiers.

In particular, the com positions of this invention also preferably contain one or more nonionic emulsifiers, each having an HLB of at least about 10, preferably at least about 11. Preferably such high HLB emulsifiers are present at a total level of from about 0.5% to about 2.0%, more preferably from about 0.6% to about 1.5%, more preferably from about 0.8% to about 1.0% (by weight of core composition). Mixtures of such high-HLB emulsifiers are preferred, particularly mixtures wherein at least one emulsifier has an HLB of at least about 12, preferably at least about 15. Such preferred pharmaceutical compositions are described in U.S. Patent Application Serial No. (P&G Case 3571), fied October 6, 1986 (incorporated by reference herein).

The core compositions of this invention may also contain one more more low-HLB emulsifiers (i.e., emulsifiers having HLB values less than about 10), particularly in order to improve rheology of the compositions in the mouth ("mouth feel"). Preferably, the present core compositions contain from about 0.1% to about 1.0%, preferably from about 0.1% to about 0.5% of a low-HLB emulsifier. The type and amount of emulsifiers useful in the present invention may be selected in order to obtain compositions with preferred melting viscosities, as described above. Such emulsifiers and other optional components useful in preferred compositions of this invention are described in U.S. Patent Application Serial No. (P&G Case 3572), fied October 6, 1986, incorporated by reference herein.

As will be appreciated by those skilied in the art, the lipid base material of the present composition may be present in any of a number of crystal forms, or polymorphs. For compo- [illegible] POP fat is utilized as the lipid base material, it is preferred that the fat be

present in the beta-prime-2 or beta-3 polymorph state. The crystal structure of the lipid base material useful herein may be affected by a variety of factors, as can be ascertained by one of skill in the art. Such factors include the presence of solids in the composition, the presence of emulsifiers, the processing conditions (particularly cooling temperatures and rates), and the particular lipid base material employed.

A preferred optional component in molded tablets of this invention (i.e., compositions that are formed upon solidification of a heated liquid composition after pouring into a suitable mold) is a "tempering aid". Such materials aid in the formation of a desired crystal structure for the lipid components of the present composition, such that the composition has a desired uniform, smooth, non-gritty texture and appearance. Tempering aids are preferably included at a level of from about 0.2% to about 2%. Among tempering aids useful herein are mixtures of mono- and diglycerides, such as Dur-Em 127 (manufactured by Durkee Foods, Division of SCM Corporation) and triglyceride mixtures, such as Cessa 60 (manufactured by Friwessa).

Preferably, the core composition contains less than about 1% of materials that are liquid at ambient conditions in addition to any liquid components in the lipid material. More preferably, these core compositions contain less than 0.5% of such additional liquid materials.

Other preferred optional components useful herein include flavorants and sweeteners, at levels of from about 0.01% to about 1.0%. Colorants may be included at typical levels of from about 0.01% to about 0.5%.

The present compositions also preferably contain, as a part of the core composition, a "pharmaceutical active material", i.e., a material which is intended to have a physiologic effect on the human or lower animal to whom the composition is administered. Pharmaceutical active materials particularly useful in the chewable tablet formulations of this invention include those actives which become bioavaiable and/or have their site of action in the mouth or stomach. The rapid dispersion of such active materials in the saliva, as afforded by the present chewable tablets, is particularly advantageous. Am ong such active materials are the analgesics, such as aspirin and acetaminophen, and materials useful in the treatment of gastrointestinal disorders.

Among the pharmaceutical active materials particularly useful in the compositions of this invention are the bismuth salts and the metallic antacid salts. These materials are preferably present at a level of from about 10% to about 65% of the core composition. Such bismuth salts include, for example, bismuth aluminate, bismuth citrate, bismuth nitrate, bismuth subcarbonate, bismuth subgalate, bismuth subsalicylate, and mixtures thereof. A particularly preferred bismuth salt is bismuth subsalicylate.

Metaliic antacid salts useful herein include, for example, aluminum carbonate, aluminum hydroxide, aluminum phosphate, aluminum hydroxycarbonate, dihydroxy aluminum sodium carbonate, aluminum magnesium glycinate, dihydroxy aluminum amino acetate, dihydroxy aluminum aminoacetic acid, calcium carbonate, calcium phosphate, aluminum magnesium hydrated sulfates, magnesium aluminate, magnesium alumino silicates, magnesium carbonate, magnesium glycinate, magnesium hydroxide, magnesium oxide, magnesium trisiicate, and mixtures thereof. Aluminum magnesium hydroxide sulfate (also known as magaldrate) is a preferred metallic antacid salt useful herein.

Coating Compositions

The compositions of this invention contain at least three coating layers, comprising a base coating, a sealant coating, and a structural coating. These compositions may also contain additional coating layers. As used herein, the term "coating" refers to a material or combination of materials that envelops a tablet (or a coated tablet) such that essentialiy all surfaces of the tablet (or coated tablet) are covered by the coating material. Preferably the coatings of this invention are essentialy uniform, i.e., of essentially equal depth or thickness over all surfaces of the underlying tablet. Each coating may be comprised of multiple layers of the same or essentially identical composition.

The coatings of this invention may contain optional materials in addition to the essential components described below. Such optional ingredients include, for example, active materials, emulsifiers, colorants, sweeteners and flavorants.

Base Coating:

The present compositions contain a base coating, which is in direct physical contact with the core composition. This base coating comprises a binder and a sugar material. As described below, the base coat is applied by covering the core composition with an aqueous solution of the binder. The tablet is then covered with the sugar material which adheres to the binder.

The binder is present at a level of from about 0.5% to about 2%, preferably from about 0.6% to about 1%. The binder material may be any material which adheres to the core composition and, after application, remains sufficiently sticky to adhere an essentially uniform coating of the sugar material. Such binder materials among those useful herein include corn syrup, sorbitol solutions, polyvinyl pyrrolidone solutions, hydrogenated corn syrup solutions, and mixtures

thereof. Hydrogenated corn syrup is a particularly preferred binder. Hydrogenated corn syrup is commercially available, for example, as Lycasin (sold by Roquette Corporation).

The sugar material is present at a level of from about 1.5% to about 7%, preferably from about 1.5% to about 4%, more preferably from about 1.9% to about 3.5%. As used herein "sugar material" refers to finely-divided, particulate sugars and sugar-like materials. Sugar materials among these useful herein include powdered sucrose, sorbitol, mannitol, and mixtures thereof. Mannitol is a particularly preferred sugar material.

Seal Coating:

The present compositions contain a seal coating, which is in direct contact with the base coat. The seal coating is comprised of one or more film-forming materials that are preferably soluble in both aqueous and organic solvents. Such film-forming materials are described in Marshali, "Solid Oral Dosage Forms", *Modern Pharmaceutics*, Volume 7 (Banker and Rhodes, editors), 359-427 (1979), incorporated by reference herein. Film-forming materials among those useful herein include methylceiulose, hydroxypropyl cellulose, hydroxypropyl-methyl cellulose, sodium carboxymethyl cellulose, povidone, and mixtures thereof. Hydroxypropyl cellulose is a preferred seal coating material

Structural Coating:

The compositions of this invention also contain a structural coating, which is in direct contact with the seal coating. The structural coating is comprised of a sugar material. Such sugar materials include, for example, sucrose, sorbitol and mixtures thereof. Sorbitol is a preferred sugar material for use in the structurai coating.

Optional Coatings:

The compositions of this invention may contain additional coatings. Preferably, for example, these compositions contain an outer coating of a film-forming material, in direct contact with the structural coating. The outer coating is preferably present at a level of from about 0.4% to about 1%, preferably from about 0.4% to about 0.6%. The film-forming materials among those useful in an optional outer coating are as described above for use in the sealant coating.

Methods

Core Composition:

The chewable tablet core compositions of this invention may be made by either compression or molding techniques. Compression techniques generaliy involve admixture of materials in an essentially dry state, foliowed by compression in a desired tablet form, under pressure. Molding techniques generaiy involve admixture of components in an essentialiy liquid form, foliowed by pouring into a desired tablet mold and cooling to a solid, or semi-solid form. The core compositions of this invention are preferably in molded form.

The lipid base material used in molded compositions of the present invention is preferably in a stable crystal form, such that the composition is comprised of stable crystals less than about 5 microns, preferably from about 1 to about 2 microns, in size, and the composition has a uniform, smooth, non-gritty appearance and rheology. Such parameters, and the factors which influence them, are analogous to parameters that are well known in the chocolate confectionery arts. As discussed above, materials may be added to the present compositions which aid in obtaining a preferred. stable crystal structure, or "temper". Processing conditions for making molded compositions are also critical, and are preferably controlled to yield a preferred tempered composition. Such "tempering", for compositions utilizing POP fat as a lipid base material, typically involves cooling of the product in liquid form, to a temperature of approximately 22°C. This cooling induces formation of a variety of crystals of different melting points. The composition is then heated, with stirring, to approximately 29.5°C, melting the undesired lower-melting crystals. (The fluid product at this point is thereby "seeded" with higher-melting crystals.) The fluid product is then poured into molds, vibrated to remove air bubbles, and slowly cooled to solidify the com position into a product having the desired crystal form.

Coatings:

The essential coatings of the present invention are made by a process generally comprising the steps of:

(a) coating the core composition with a base coating comprising a binder and a sugar material;

(b) coating said base coat with a sealant coating comprising a film-forming material; and

(c) coating said sealant coating with a structural coating comprising a sugar material.

Specific techniques for applying the essential coatings are known in the art. Coating techniques are described, for example, in Marshali, "Solid Oral Dosage Forms", *Modern Pharmaceutics, Volume 7* (Banker and Rhodes, editors), 359-427 (1979) and J. R. Eliis et al., "Tablet Coating", *The Theory and Practice of Indus-trial Pharmacy* (L. Lachman et al., editors, 2d edition), 359-388

(1976), both incorporated by reference herein. The drying steps used in coating the present compositions preferably employ air drying at ambient or near-ambient conditions. Preferably, the tablets are dried, as required in each coating step, at a temperature of from about 20°C to abut 25°C.

Prior to the base coating step (a), the lipid-containing core tablets are preferably treated so as to remove substantially all surface irregularities and angular edges. This treatment may be by mechanical tumbling, such as by rotating the cores in a coating pan.

The base coating step (a) may be performed by first adding the binder solution to the tablet cores, in a coating apparatus. A conventional pan coater may be used, for example. Sufficient binder is applied to ensure essentially complete and uniform coating of the cores, whie avoiding substantial excess. The particulate sugar material, preferably mannitol, is sieved and applied to the tablet cores while rotating in the pan. The base coated tablets are then removed from the pan, and allowed to dry.

The sealant coating step (b) may be performed by first dissolving the film-forming material, preferably hydroxypropyl celiulose, in a suitable solvent. Suitable organic solvents include, for example, lower alcohols, chloroform, acetone, methyl ethyl ketone, methylene chloride, and mixtures thereof. Acetone is a preferred organic solvent when hydroxypropyl cellulose is used as the film-forming material. The film-forming material is applied using, for example, a fluidized bed coating apparatus or a perforated pan coater. All solvent is eliminated from the coating apparatus, and the sealant coated tablets are dried.

The structural coating step (c) may be performed by adding a sorbitol solution (i.e., as an approximately 70% solution of sorbitol in water) to a coating apparatus, such as a pan coater. The sorbitol is added slowly, allowing the water to evaporate. Warm air may be directed over the tablets to aid in drying. After the desired level of structural coating is applied, the coated tablets are allowed to dry.

Optional coatings, such as a top coating, may be applied by conventional techniques. For example, a top coating of a film-forming material may be applied using the techniques generally used for the sealant coating step (b), as described above.

The following non-limiting Example illustrates a composition, process and use of the present invention.

EXAMPLE 1

A coated antacid composition according to this invention was made comprising:

Component	% Bulk Composition	% Final Tablet
POP fat	35.942	30.000
sucrose	26.119	21.800
magaldrate	35.703	29.800
Cessa 60[1]	0.994	0.830
Myrij 52[2]	0.503	0.420
Caprol PGE 860[3]	0.395	0.330
Polyaldo HGDS[4]	0.252	0.210
flavorant	0.092	0.077
	100.000	
(Coating)		
sorbitol solution[5]		10.700
Lycasin[6]		1.060
mannitol		4.023
Klucel EF[7]		0.750
		100.000

1. triglyceride mixture, tempering aid, manufactured by Friwessa.
2. polyoxyl (40) stearate, nonionic emulsifier, HLB=16.9, manufactured by ICI Americas, Inc.
3. decaglycerol mono-dioleate nonionic emulsifier, HLB=11.0, manufactured by Capital City Products Co., division of Stokely-Van Camp, Inc.
4. hexaglycerol distearate nonionic emulsifier, HLB=7.0, manufactured by Glyco, Inc.
5. 70% solution.
6. hydrogenated glucose syrup, manufactured by Roquette Corporation.
7. hydroxypropyl cellulose gum, manufactured by Hercules Chemical Co.

Lipid-containing core compositions, comprised as above, were made by mixing the active material and dispersant material at a temperature of approximately 40°C. Approximately 55% of the lipid material was melted, at approximately 40°C. The melted lipid material was then added to the active/dispersant mixture, maintaining the temperature at approximately 40°C, whie mixing. This mixture was then passed through a roll mill.

The hexaglycerol distearate and the crystal growth modifier were then admixed with the remaining lipid material, and the mixture heated to approximately 50°C. The roli milled lipid/active/dispersant mixture was then added to the lipid/emulsifier mixture at a temperature of approximately 50°C to 55°C. The remaining emulsifiers were then mixed with ethanol and admixed with the lipid containing mixture.

This mixture was then cooled and tempered. The composition was then molded into tablet forms, forming lipid-containing core tablets.

Approximately 2 to 4 kiograms (kg) of the lipid-containing core tablets were placed in a 25.4 centimeter (10 inch) coating pan. The pan was rotated at full speed for approximately 40 minutes, smoothing the cores and essentialiy eliminating sharp edges.

Approximately 1.5 to 2.5 kg of the core tablets were then placed in a clean coating pan. The cores were evenly coated with Lycasin, in the rotating pan. The mannitol was sieved through a 1.8 mm screen and was added slowly until the surfaces of the cores were covered. The pan was rotated for a maximum of approximately 5 minutes during this process. The base coated tablets were then dried for at least about 12 hours at approximately 24°C and 55% relative humidity. Dust was removed from the dried tablets by fluidizing in a Glatt GPCG 17.8 cm (7 inch) fluid bed coater for approximately 1 minute.

A Glatt fluid bed coater was preheated to have an air inlet temperature of approximately 26°C. A solution of Klucel was prepared by dissolving the Klucel in acetone and 95% alcohol (The final solution concentration was approximately 10% Klucel, 72% acetone, 17% alcohol, 1% water.) A quantity of the Klucel solution was then added (allowing for approximately 15% loss during the process) to the pump reservoir of the apparatus. Approximately 3.8 kg of the base coated tablets were placed in the coater and the Klucel solution applied with an atomizing air pressure of approximately 1.5 bars. After all of the Klucel solution was applied, the seal coated tablets were dried in the coater for approximately 1 minute. The tablets were removed and further dried in an open pan for approximately 1 to 2 hours, at approximately 24°C and 55% relative humidity.

Approximately 1.9 kg of the seal coated tablets were placed in a clean 25.4 cm (10 inch) coating pan. The sorbitol solution was then weighed, allowing for 10% loss during the coating process, and added in small increments. The tablets were dried during this process, with warm air, as the pan rotated. (The sorbitol solution was added initially in very small increments to avoid excess wetting and uneven coating.) After all of the sorbitol was applied, the tablets were rotated for an additional time (approximately 10 to 15 minutes), under cooler air. The tablets were further dried in an open pan at approximately 24°C and 55% relative humidity. An outer coating of Klucel was then applied, using a procedure analogous to that described above for the seal coating.

Finished coated tablet compositions, comprised as above, are administered to a human subject experiencing heartburn, and are effective in reducing the severity of symptoms. The compositions are stable upon storage at elevated temperatures.

CLAIMS

1. A coated tablet composition comprising a lipid-containing core composition and three coatings, said coatings comprising:

(1) a base coating, in direct contact with said core composition, comprising a binder and a sugar material;

(2) a sealant coating, in direct contact with said base coating, comprising a film-forming material and

(3) a structural coating, in direct contact with said sealant coating, comprising a sugar material.

2. A coated tablet composition, according to Claim 1, comprising from about 50% to about 90% of said core composition.

3. A coated tablet composition, according to Claim 2, wherein said base coating binder is present at a level of from about 0.5% to about 2%.

4. A coated tablet composition, according to Claim 3, wherein said binder comprises hydrogenated corn syrup.

5. A coated tablet composition, according to Claim 3, wherein said base coating sugar material is present at a level of from about 1.5% to about 5%.

6. A coated tablet composition, according to Claim 5, wherein said base coating sugar material comprises mannitol.

7. A coated tablet composition, according to Claim 2, wherein said film forming material is present at a level of from about 0.2% to about 1%.

8. A coated tablet composition, according to Claim 7, wherein said film forming material comprises hydroxypropyl cellulose.

9. A coated tablet composition, according to Claim 2, wherein said structural coating sugar material is present at a level of from about 5% to about 30%.

10. A coated tablet composition, according to Claim 9, wherein said structural coating sugar material comprises sorbitol.

11. A coated tablet composition, according to Claim 2, additionally com prising a top coating, in direct contact with said structural coating, comprising a film-forming material.

12. A coated tablet composition, according to Claim 2, wherein said core composition comprises a lipid material, and a dispersant material.

13. A coated tablet composition, according to Claim 12, wherein said lipid material is present at a level of from about 25% to about 40% of said core composition.

14. A coated tablet composition, according to Claim 13, wherein said dispersant material is present at a level of from about 20% to about 35% of said core composition.

15. A coated tablet composition, according to Claim 15, additionaliy comprising an emulsifier.

16. A coated tablet composition, according to Claim 12, additionaliy comprising a tempering aid.

17. A coated tablet composition, according to Claim 12, additionaiy comprising a safe and effective amount of a pharmaceutically active material.

18. A coated tablet composition, according to Claim 17, wherein said pharmaceutical active material is useful in the treatment of gastrointestinal disorders.

19. A coated tablet composition, according to Claim 18, wherein said pharmaceutical active material is an metallic antacid salt.

20. A coated tablet composition, according to Claim 18, wherein said pharmaceutical active material is a bismuth salt.

21. A process for m aking a coated tablet composition containing a lipid-containing core, comprising the steps of:

(a) coating said core with a base coating comprising a binder and a sugar material;

(b) coating said base coating with a sealant coating comprising a film-forming material; and

(c) coating said sealant coating with a structural coating comprising a sugar material.

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